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Diagnostic accuracy of culture-based and PCR-based detection tests for methicillin-resistant *Staphylococcus aureus*: a meta-analysis

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Abstract

A systematic review and meta-analysis were performed to determine and compare the sensitivity and specificity of PCR-based and culture-based diagnostic tests for methicillin-resistant *Staphylococcus aureus* (MRSA). Our analysis included 74 accuracy measurements from 29 publications. Nine tests were evaluated: the PCR-based Genotype MRSA Direct and IDI-MRSA, the chromogenic media CHROMagar, Chromogenic MRSA Medium, MRSA ID, MRSA Select and ORSAB, and the nonchromogenic culture media MSA-Cefoxitin and MSA-Oxacillin. For four chromogenic media, incubation periods of 18–24 and 48 h were evaluated. Considerable heterogeneity was detected in most analyses. A significantly higher sensitivity was found for the overall PCR pooled estimate (92.5; 95% CI 87.4–95.9) and the chromogenic media after 48 h of incubation (87.6; 95% CI 82.1–91.6) compared to the overall sensitivity of chromogenic media after 18–24 h (78.3; 95% CI 71.0–84.1). The specificity of chromogenic media after 18–24 h (98.6; 95% CI 97.7–99.1) was higher than the specificity of PCR (97.0; 95% CI 94.5–98.4) but declined after 48 h of incubation (94.7; 95% CI 91.6–96.8). The most sensitive chromogenic medium after 18–24 h of incubation was Chromogenic MRSA Medium (sensitivity: 89.3; 95% CI 72.8–96.3), whereas the most specific chromogenic medium after 18–24 h of incubation was MRSA Select (specificity: 99.4; 95% CI 98.6–99.7). After 48 h of incubation, MRSA Select had the highest sensitivity (93.2; 95% CI 83.5–97.0), whereas CHROMagar had the highest specificity (96.4; 95% CI 91.3–98.5). This meta-analysis showed statistically significant differences in diagnostic accuracy between several of the tests and the test methods evaluated. A reduction of the incubation time of chromogenic media (from 48 to 18–24 h) increases specificity but reduces sensitivity.

Keywords: Diagnostic accuracy, meta-analysis, methicillin-resistant *Staphylococcus aureus* MRSA, nosocomial infections, PCR and culture screening

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Introduction

Staphylococcus aureus is one of the most common causes of nosocomial and community-acquired infections. The first methicillin-resistant *Staphylococcus aureus* (MRSA) strain was detected in 1960 [1], 1 year after the introduction of methicillin in 1959. Methicillin resistance is mediated by the penicillin-binding protein 2a (PBP-2a), a variant of the PBP-2

protein, encoded in the *mecA* gene. Ever since the 1980s, incidences of infections caused by MRSA as well as asymptomatic carriage by hospitalized patients, have increased dramatically worldwide [2–4]. Carriage of MRSA is an important risk factor for subsequent infection, with the anterior nares being the primary predilection site [5].

Although proportions of nosocomial MRSA infections among all *S. aureus* infections have reached high levels in many countries, a number of countries, such as the Netherlands and the Scandinavian countries [4], have maintained low prevalence rates with stringent infection control policies. These policies consist of a combination of measures, such as isolation of identified MRSA carriers, decolonizing patients, admission screening of high-risk patients with pre-emptive isolation, screening of all contact patients and health care

workers (HCW) and unexpected (index) cases, furloughing of HCWs from work and closing of wards in case of uncontrolled spread. Bootsma et al. [6] recently investigated the individual contribution of the components of this Dutch *search and destroy* policy [7], indicating that admission screening of high-risk patients in combination with (pre-emptive) isolation could be highly beneficial, even in high-prevalence settings. When performing such a strategy, rapid detection is crucial, limiting transmission risks and the costs of isolation. Conventional microbiological cultures have a diagnostic delay of at least 48 h, which increases when broth enrichment of material is used. Several novel and faster diagnostic tests to screen for MRSA have been introduced in the last 5 years.

To select an appropriate test for a hospital admission screening programme, one also needs to consider a test's specificity, sensitivity and price, in addition to the turnaround time (TAT). Obviously, false positive results will drive up isolation costs, whereas false negative results will increase the risks of transmission but, on closer examination, the interplay of the test characteristics with the local conditions within different screening strategies becomes quite complex. Mathematical modelling studies can inform hospital decision-makers on cost-effective combinations of tests and screening strategies within a particular setting, although such studies require accurate estimates of diagnostic accuracy.

The present study aimed to determine and compare the sensitivity and specificity of nine commercially available diagnostic MRSA tests using systematic review and meta-analysis techniques in line with the PRISMA guidelines [8], including: the PCR-based Genotype MRSA Direct and IDI-MRSA, CHROMagar, Chromogenic MRSA Medium, MRSA ID, MRSA Select, ORSAB, MSA-Cefoxitin and MSA-Oxacillin.

Materials and Methods

Search strategy

A literature search of Medline and Embase was conducted to identify publications that were published before or during 2008. Keywords and Boolean operators used for searches were 'MRSA' OR ('resistant' AND '*Staphylococcus aureus*') AND 'detection' AND ('sensitivity' OR 'specificity'). No restrictions were set for language or publication type. The reference lists of enrolled publications were reviewed until no further new publications were identified.

Inclusion criteria

Nine different commercially available screening tests were assessed with incubation times ≤ 48 h: two PCR-based tests, IDI-MRSA (BD Diagnostics, Sparks, MD, USA) and Genotype

MRSA direct (HAIN Lifescience, Nehren, Germany), five chromogenic media, CHROMagar (BD Diagnostics; and CHROMagar Microbiology, Paris), Chromogenic MRSA Medium (Oxoid, Hampshire, UK), MRSA ID (BioMérieux, La-Balme-les-Grottes, France), MRSA Select (Bio-Rad, Marnes-la-Coquette, France) and ORSAB (Oxoid, Hampshire, UK) and two nonchromogenic culture media, MSA-Cefoxitin and MSA-Oxacillin (various sources).

Titles and abstracts of all publications were read by two reviewers (GAAH and JML). The full text was obtained if the abstract suggested a diagnostic accuracy study of one or more PCR-based or culture-based MRSA tests. Publications were eligible for inclusion if: (i) the results were reported as true negative (TN), true positive (TP), false positive (FP) and false negative (FN) on screened sample level, or if these outcomes were derivable from the presented data; (ii) more than 80% of the screened samples consisted of axilla, groin, nose, perineum and throat samples; and (iii) if samples were not taken from a strain library. The latter two restrictions were set to reduce heterogeneity and to exclude samples that were not representative of samples obtained through hospital admission screening. No restrictions were set for the clinical reference standard method applied.

Validity assessment

Quality assessment of included publications was performed using the QUADAS tool [9]. Because the QUADAS tool does not incorporate a quality score for various reasons, no regression analysis was performed on publication quality and diagnostic performance of tests evaluated and no publications were excluded based on quality assessment.

Ethical considerations

This study did not require the approval of an ethics committee.

Data extraction

Data were extracted from each included publication by reviewers JML and GAAH and included TN, TP, FP and FN. Data were collected in 2×2 tables and subsequently pooled by test and category (PCR-based, chromogenic and nonchromogenic culture media). The five chromogenic agar-based tests were further subcategorized according to incubation times of 18–24 h and 48 h. Subgroups were created for nasal swabs and manufacturer (CHROMagar; BD Diagnostics and CHROMagar Microbiology) if three or more publications were available.

Quantitative data synthesis

The statistical analysis was carried out using R, version 2.8.1 [10] and SAS software [11]. The hypothesis of inter-study

heterogeneity was statistically tested using the *i*-squared statistic [12]. Values of *i*-squared equal to 25%, 50% and 75% were considered to represent low, moderate and high levels of heterogeneity, respectively. We further investigated the causes of heterogeneity by means of subgroup analyses. Pooled sensitivity, specificity and 95% confidence intervals were estimated for each test using the bivariate method described by Reitsma *et al.* [13]. Using this method, we were also able to perform pairwise investigations of differences between the sensitivity and specificity of all main pools. $p < 0.05$ was considered statistically significant.

To assess publication bias, we used the relation between the diagnostic odds ratio (DOR) and the effective sample size (ESS) [14]. In particular, a regression of the natural logarithm of DOR against $1/\text{ESS}^{1/2}$, weighted by ESS was performed. $p < 0.05$ was considered statistically significant.

Results

Selection flow

We identified 599 publications, of which 28 met our inclusion criteria [15–42]. One additional eligible publication [43] was detected through the reference list of an enrolled publication (Fig. 1). The 29 enrolled publications (Table 1) yielded a total of 90 accuracy measurements, of which 16 did not include nor allow derivation of TN and FP. Because our statistical methodology requires both sensitivity and specificity estimates, those 16 comparisons were excluded.

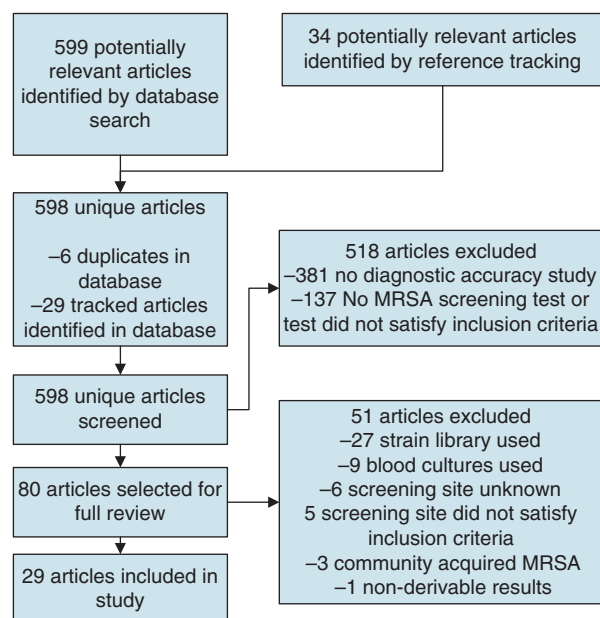


FIG. 1. Flow chart of the article selection process.

Study characteristics

The number of accuracy measurements included in the main pools was 15 for PCR-based, 28 for chromogenic 18–24 h, 24 for chromogenic 48 h and seven for nonchromogenic 48-h culture tests (Table 2). Our subgroup analysis on nasal swabs included a total of 25 accuracy measurements. The average number of samples in the selected accuracy measurements included was 936 (95% CI 0–2215) and the average number of MRSA-positive samples (TP + FN) was 92 (95% CI 36–147). The most commonly encountered shortcomings identified by the QUADAS tool were failure to blind reference test readers to results of the index test ($n = 29$), partial verification bias ($n = 27$) and differential verification bias ($n = 23$). The most commonly used reference standards were susceptibility testing with agar diffusion ($n = 13$), *mecA* PCR ($n = 15$) and latex agglutination of PBP2a ($n = 9$) (Table 1).

Quantitative data synthesis

The overall pooled estimates of the test sensitivities and specificities are shown in Table 2. Receiver-operating characteristic plots including the individual accuracy measurements grouped per diagnostic test are shown in Figs 2, 3 and 4. Bivariate summary estimates of sensitivity and specificity and 95% confidence ellipses of each of the evaluated diagnostic tests are graphically represented in Figs 5, 6 and 7.

Comparing test methods, a significantly higher sensitivity was found for the overall PCR pooled estimate (92.5; 95% CI 87.4–95.9) compared to the overall estimate of chromogenic media after 18–24 h (78.3; 95% CI 71.0–84.1) and 48 h of incubation (87.6; 95% CI 82.1–91.6). The specificity of chromogenic media after 18–24 h (98.6; 95% CI 97.7–99.1) is higher than the specificity of PCR (97.0; 95% CI 94.5–98.4) but declines after 48 h of incubation (94.7; 95% CI 91.6–96.8). Culture-based tests showed sensitivity comparable with other test methods evaluated but performed worse with respect to specificity.

Among PCR-based tests, the sensitivity of IDI MRSA was higher than that of Genotype MRSA, although the specificities of these two tests were comparable.

Among the chromogenic media after 18–24 h of incubation, Chromogenic MRSA Medium had the highest sensitivity (89.3; 95% CI 72.8–96.3), whereas MRSA Select had the highest specificity (99.4; 95% CI 98.6–99.7) (not significant). Among the chromogenic media after 48 h of incubation, MRSA Select had the highest sensitivity (93.2; 95% CI 83.5–97.0), whereas CHROMagar had the highest specificity (96.4; 95% CI 91.3–98.5) (not significant).

The vast majority of the 44 data pools evaluated was found to be moderately ($n = 5$), or highly heterogeneous

TABLE 1. Summary of characteristics of selected articles

Reference	Location and year	Methods evaluated and included*	Total number of specimens screened/number of positives (% positive)	Specimen origin	Number of patients (mean number of specimens per patient)	Broth enrichment used in reference method	Reference method MRSA-positives	Unsatisfied QUADAS items.	QUADAS items unclear to be satisfied
Apfalter et al. [15]	Austria, 2002	ORSAB ^c , MSA-Oxacillin ^b	579/236 (40.8)	119 axillae, 70 inguinal, 131 nares, 60 throat, wounds 61, other 138	83 (7.0)	Yes	PCR <i>mecA</i>	5, 6, 11	
Ben Nsira et al. [16]	France, 2006	MRSA Select ^c , ORSAB ^c	666/99 (14.9)	648 nasal, other 14	Not specified	No	PCR <i>mecA</i>	5, 6, 11, 13	
Bishop et al. [17]	Australia, 2006	IDI-MRSA	576/79 (13.7)	192 groin, 192 nares, 192 combined groin-nares	192 (3.0)	Yes	PCR <i>mecA</i>	5, 6, 11	
Boyce et al. [18]	USA, 2007	IDI-MRSA	286/69 (24.1)	286 nares	286 (1.0)	Yes	Latex agglutination of PBP2a	5, 6, 7	11
Cherkaoui et al. [19]	Switzerland, 2007	MRSA ID ^c , MRSA Select ^c , ORSAB ^c	247/70 (28.3)	247 combined nostril-groin	247 (1.0)	Yes	PCR <i>mecA</i>	5, 9, 11, 13	6
Compemolle et al. [20]	Belgium, 2007	CHROMagar ^c , MRSA ID ^c , ORSAB ^c	366/30 (8.2)	53 nose, 153 perineum, 116 throat, other 43	Not specified	No	PCR <i>mecA</i>	2, 5, 11, 12	1
De San et al. [21]	Belgium, 2007	IDI-MRSA	997/100 (10.0)	522 nares, 206 perineum, 212 throat, other 60	466, 1000 specimens (2.1)	Yes	Phenotypic (agar diffusion)	3, 4, 7, 13	11
Desjardins et al. [22]	Canada, 2006	IDI-MRSA	285/74 (26.0)	53 nasal, 28 rectal, 174 combined nasal-rectal, other 32	Not specified (2.0-4.0)	Yes	Phenotypic (agar diffusion) and Latex agglutination of PBP2a	2, 3, 5, 6, 11	
Dias et al. [23]	Brazil, 2004	MSA-Oxacillin ^b , ORSAB ^b	224/32 (14.3)	224 nares	Not specified	No	PCR <i>mecA</i> and Latex agglutination of PBP2a	2, 5, 6, 11	
Flayhart et al. [24]	USA, 2005	CHROMagar ^c	2015/146 (7.2)	2015 anterior nares	Not specified (1.0)	No	PCR <i>mecA</i>	5, 6, 11	
Gilpin et al. [25]	UK, 2007	IDI-MRSA	1440/40 (2.8) and 346/26 (7.5)	720 nasal swabs, 720 skin swabs and 173 nasal swabs, 173 skin swabs	720 (2.0) and 173 (2.0)	No	Phenotypic (agar diffusion)	2, 5, 7, 8, 9, 11	6
Han et al. [26]	USA, 2007	CHROMagar ^c	340/39 (11.5)	340 nasal	Not specified	No	Phenotypic (agar diffusion)	5, 11	6
Hoffelder et al. [27]	Germany, 2006	Genotype MRSA Direct	508/37 (7.3)	209 nose, 101 throat, 80 skin, 46 groin, 34 wound, 12 axilla, other 26	242 (2.1)	Yes	Latex agglutination of PBP2a, PCR <i>mecA</i>	3, 5, 9, 11	6
Hope et al. [28]	Australia, 2004	MSA-Oxacillin ^b	256/34 (13.3)	129 groin, 115 nose, other 12	Not specified	Yes	MSAO-broth	2, 3, 5, 6, 11	
Huletsky et al. [29]	Canada, 2005	IDI-MRSA	331/81 (24.5)	331 nasal	162 (2.0)	No	Phenotypic (agar diffusion)	5, 6, 11	
Johnson et al. [30]	UK, 2006	MSA-Oxacillin ^b	1382/170 (12.3)	1382 nasal	Not specified	No	Phenotypic (agar diffusion)	2, 5, 11, 13	6
Krishna et al. [31]	UK, 2008	Chromogenic MRSA ^a medium, MRSA Select ^a , ORSAB ^c	632/63 (10.0) and 720/83 (11.5)	72% groin, nose, throat and 95% groin, nose, throat, wound	205 (3.1) and 250 (2.9)	No	Latex agglutination of PBP2a	2, 5, 6, 11	
Louie et al. [32]	Canada, 2006	MRSA Select ^c , MSA-Cefoxitin ^c	4853/125 (2.6)	2483 nares, 2312 perineal, other 58	1883, 6119 specimens (3.2)	No	Phenotypic (agar diffusion) and Latex agglutination of PBP2a	2, 5, 11	6
Loulergue et al. [43]	France, 2006	CHROMagar ^c	831/119 (14.3)	831 nasal	321 (2.6)	No	PCR <i>mecA</i>	2, 5, 9, 11, 12	1, 6
Nahimana et al. [33]	Switzerland, 2006	CHROMagar ^c , MRSA ID ^c , MRSA Select ^c , ORSAB ^c	466/102 (21.9)	127 nose, 125 perineum, 121 throat, 49 wound, other 44	98 (4.8)	No	Phenotypic (agar diffusion) and Latex agglutination of PBP2a	5, 6, 7, 11	
Oberdorfer et al. [34]	Germany, 2006	IDI-MRSA	304/12 (3.9)	304 nasal	304 (1.0)	Yes	Phenotypic (agar diffusion) and Latex agglutination of PBP2a/PCR <i>mecA</i> for discrepant results	5, 6, 11	
Paule et al. [35]	USA, 2007	IDI-MRSA	399/49 (12.3)	399 nasal	Not mentioned	Yes	PCR <i>mecA</i>	5, 11	
Reyes et al. [36]	Canada, 2007	Chromogenic MRSA Medium ^a , MRSA Select ^a	2097/200 (9.5)	1056 nasal, 950 perianal, 70 wound, other 21	831 (2.5)	No	PCR <i>mecA</i>	5, 13	11
Rosney et al. [37]	Ireland, 2007	IDI-MRSA	603/116 (19.2)	Groin, nose, throat	202, 606 specimens (3.0)	Yes	PCR <i>mecA</i>	6, 11	
Stoakes et al. [38]	Canada, 2006	CHROMagar ^b , MRSA Select ^b , MSA-Cofoxitin ^b , MSA-Oxacillin ^b	2125/111 (5.2)	1243 nasal, 882 perineal	Not specified	No	PCR <i>mecA</i>	5, 11	

TABLE 1. (Continued)

Reference	Location and year	Methods evaluated and included.*	Total number of specimens screened/number of positives (% positive)	Specimen origin	Number of patients (mean number of specimens per patient)	Broth enrichment used in reference method	Reference method MRSA-positives	Unsatisfied QUADAS items.	QUADAS items unclear to be satisfied
Van Hal et al. [39]	Australia, 2007	Genotype MRSA Direct, IDI-MRSA, CHROMagar ^c , MRSA ID ^c , MRSA Select ^c	101/53 (52.5)	101 nasal	205, 205 specimens (1.0)	No	Phenotypic (agar diffusion) and PCR mecA for discrepant results	2, 5, 11	
Van Loo et al. [40]	Netherlands, 2007	MRSA ID ^c , MRSA Select ^a	3000/70 (2.3)	972 nose, 968 perineum, 972 throat, 88 wound	409 (7.3)	Yes	Phenotypic (agar diffusion) and Latex agglutination of PBP2a	5, 11	6
Van Nguyen et al. [41] Warren et al. [42]	France, 2006 USA, 2004	IDI-MRSA IDI-MRSA	682/47 (6.9) 288/66 (22.9)	682 nasal 288 nasal	508 (1.3) 288 (1.0)	Yes Yes	MSAO-broth Phenotypic (agar diffusion)	3, 5, 11 5, 11	6 6

For culture tests:

^a18–24 h of incubation reported^b48 h of incubation reported^cBoth 18–24 h and 48 h of incubation reported.

($n = 39$). Sufficient data were available for subgroup analysis concerning nasal swabs for IDI-MRSA, CHROMagar and MRSA Select. Comparison of nasal swab-only data to complete data (including samples from other body sites) revealed nonsignificant differences for IDI-MRSA, CHROMagar and MRSA Select (Table 2). In general, sensitivity was slightly higher for nasal swabs only, whereas the specificity hardly changed. No significant differences were obtained for subgroup analysis of CHROMagar manufacturer (data not shown). No publication bias was discovered in the data pools of individual tests.

Discussion

This meta-analysis provides an overview of the diagnostic accuracy of MRSA screening tests reported in the literature and can be used to compare individual tests as well as testing methods.

The reduction in sensitivity estimates of the oxacillin-containing ORSAB chromogenic medium from 82.9% to 67.4%, when shortening incubation time from 48 to 18–24 h, might be caused by delayed oxacillin resistance expression [16]. The low performance of MSA-Oxacillin in terms of sensitivity might be caused by some MRSA strains that could become inhibited by the salt component of mannitol salt agar [44].

The analyses including swabs from different body sites showed a slightly (but not significantly) lower sensitivity and similar specificity for IDI-MRSA, CHROMagar and MRSA Select, compared to the analyses of nasal swabs only. This decreased sensitivity might be caused by a larger amount of competing flora or a result of lower levels of MRSA colonization at these anatomical sites [45]. This suggests that these tests can be used safely for screening of body sites other than the nares.

The most important limitation of the present study was the high level of heterogeneity of most study pools. Therefore, our estimates should be interpreted with caution. Likely causes of this heterogeneity are the differences between studies in the design (reference method, test protocol, definition of a positive result), the geographical location (diverse MRSA prevalence, local strain dominance) and the incubation time (a range of 18–24 h for chromogenic media). The causes of heterogeneity were investigated by subgroup analysis, although the level of information provided by the included studies was not sufficient for extensive subgroup analysis. We performed subgroup analysis by nasal swabs and by manufacturer, but this did not allow us to further explain the causes of heterogeneity.

TABLE 2. Pooled estimates of sensitivity and specificity with 95% confidence intervals

Screening strategy	Number of studies	Effective sample size regression test (p value)	Sensitivity (95% CI)	Specificity (95% CI)
PCR	15	–	92.5% (87.4–95.9)	97.0% (94.5–98.4)
Genotype MRSA	2	NA	83.8% (53.9–95.8)	97.7% (88.3–99.6)
IDI-MRSA	13	0.36	93.8% (88.7–96.6)	96.9% (94.2–98.4)^a
IDI-MRSA Nasal	11	0.37	94.8% (90.0–97.4)	96.7% (92.9–98.5)
Chromogenic, 18–24 h	28	–	78.3% (71.0–84.1) ^{b,c}	98.6% (97.7–99.1)
CHROMagar	6	0.10	80.3% (64.5–90.2)^{d,e}	99.0% (97.2–99.7)
CHROMagar Nasal	4	0.21	86.4% (71.4–94.2)	99.1% (96.5–99.8)
Chromogenic MRSA Medium	3	0.90	89.3% (72.8–96.3)	98.5% (94.4–99.6)
MRSA ID	4	0.11	65.1% (41.3–83.2)^{d,e,f,g,h}	98.2% (93.4–99.5)
MRSA Select	9	0.13	83.2% (71.7–90.6)^d	99.4% (98.6–99.7)
MRSA Select Nasal	3	0.18	88.4% (73.7–96.1)	99.5% (97.2–99.9)
ORSAB	6	0.47	67.4% (48.3–82.0)^{d,e,f,g,h}	95.0% (87.9–98.1)^{a,i}
Chromogenic, 48 h	24	–	87.6% (82.1–91.6)	94.7% (91.6–96.8) ^j
CHROMagar	7	0.10	88.1% (77.4–94.1)	96.4% (91.3–98.5)^a
CHROMagar Nasal	4	0.27	93.8% (84.8–97.6)	96.0% (85.6–99.0)
MRSA ID	4	0.10	83.1% (64.5–93.0)	92.9% (80.1–97.7)^{a,i}
MRSA Select	6	0.10	93.2% (83.5–97.0)	96.2% (90.4–98.5)^a
MRSA Select Nasal	3	0.15	94.1% (82.5–98.2)	93.8% (76.3–98.6)
ORSAB	7	0.43	82.9% (69.5–91.2)^d	91.8% (82.4–96.4)^{a,f,i}
Culture, 48 h	7	–	86.9% (74.7–93.7)	89.7% (77.7–95.6) ^{b,j}
MSA-Cefoxitin	2	NA	95.5% (81.4–99.0)	81.4% (46.6–95.6)^{a,d,f,i,k}
MSA-Oxacillin	5	0.24	81.7% (64.3–91.8)^d	92.1% (80.4–97.1)^{f,i,a}

The bivariate method described in detail by Reitsma et al. [13] was used to calculate and compare diagnostic accuracy estimates. NA, not available. Main pools are emphasized in bold.

^aSignificantly lower than MRSA Select 18–24 h.

^bSignificantly lower than the PCR-group.

^cSignificantly lower than the 48 h chromogenic group.

^dSignificantly lower than IDI-MRSA.

^eSignificantly lower than MRSA Select 48 h.

^fSignificantly lower than Chromogenic MRSA Medium 18–24 h.

^gSignificantly lower than CHROMagar 48 h.

^hSignificantly lower than MSA-Cefoxitin 48 h.

ⁱSignificantly lower than CHROMagar 18–24 h.

^jSignificantly lower than the 18–24 h chromogenic group.

^kSignificantly lower than MRSA ID 18–24 h.

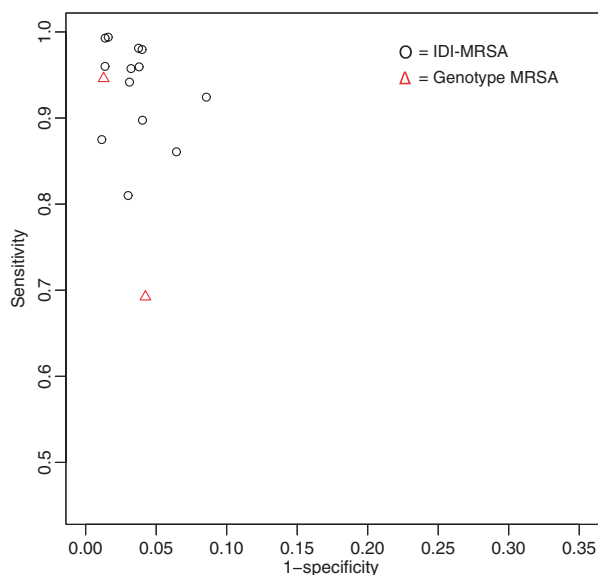


FIG. 2. Receiver-operating characteristic plot of sensitivity against 1 – specificity for the 15 PCR comparisons included in this meta-analysis.

This meta-analysis was based on indirect, unpaired accuracy measurements and did not take advantage of the strengths of several studies that included head-to-head com-

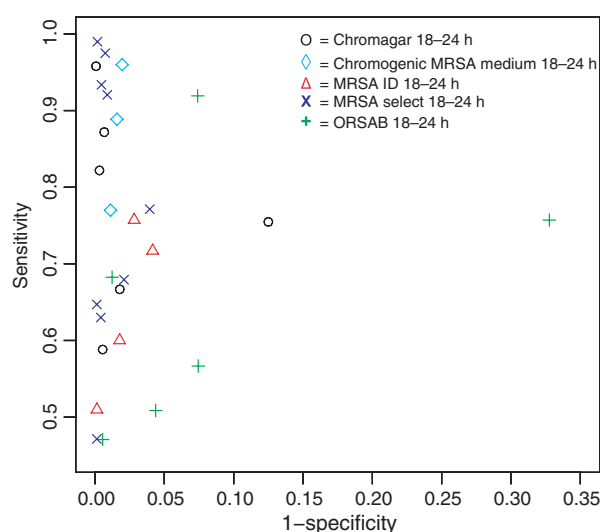


FIG. 3. Receiver-operating characteristic plot of sensitivity against 1 – specificity for the 28 18–24 h chromogenic media test comparisons included in this meta-analysis.

parisons of MRSA tests in a single series of patients. Pooling by head-to-head comparisons would have probably reduced heterogeneity but also pool sizes.

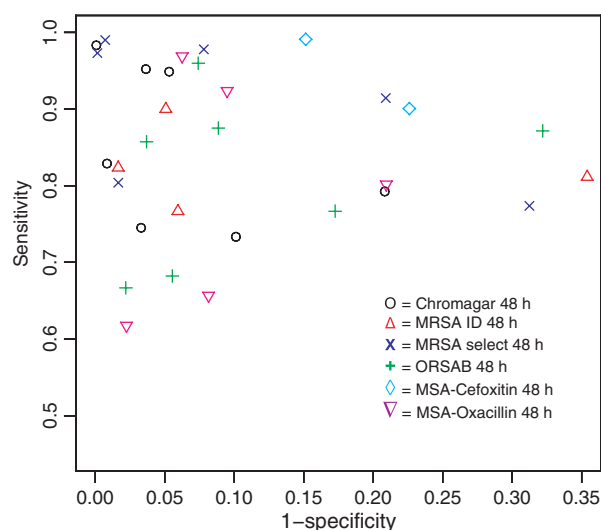


FIG. 4. Receiver-operating characteristic plot of sensitivity against $1 - \text{specificity}$ for the 31 48 h culture (both chromogenic and non-chromogenic) test comparisons included in this meta-analysis.

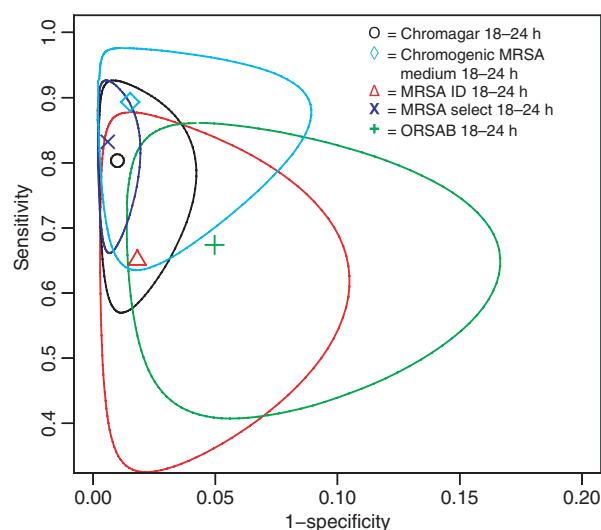


FIG. 6. Bivariate summary estimates of sensitivity and specificity for all five 18-24-h chromogenic media tests evaluated and the 95% confidence ellipses around these mean values.

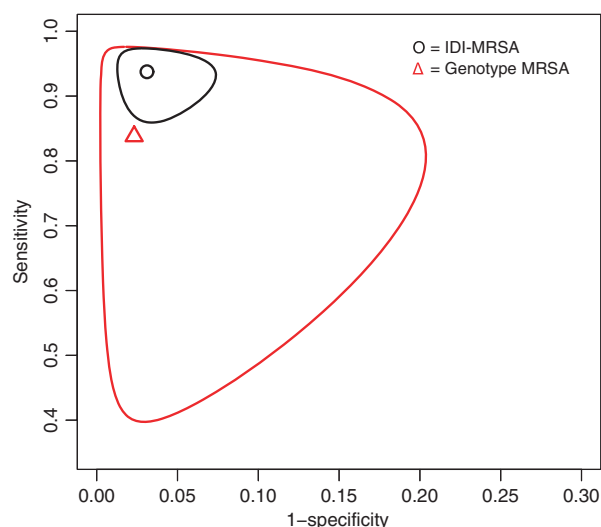


FIG. 5. Bivariate summary estimates of sensitivity and specificity for both PCR tests evaluated and the 95% confidence ellipses around these mean values.

The database keyword search may not have been optimal [46], but any missed articles are likely to have been detected through reference tracking.

In addition to diagnostic accuracy, the TAT of a test is important in a screening programme but was outside the scope of this study. A minority of studies included in our analysis reported on TAT, but often not based on an appropriate study design and not generalizable to clinical practice. Future studies on diagnostic accuracy should consider incorporating measurement of TAT in clinical practice. The choice of a test will also depend on its price. A cost-effectiveness

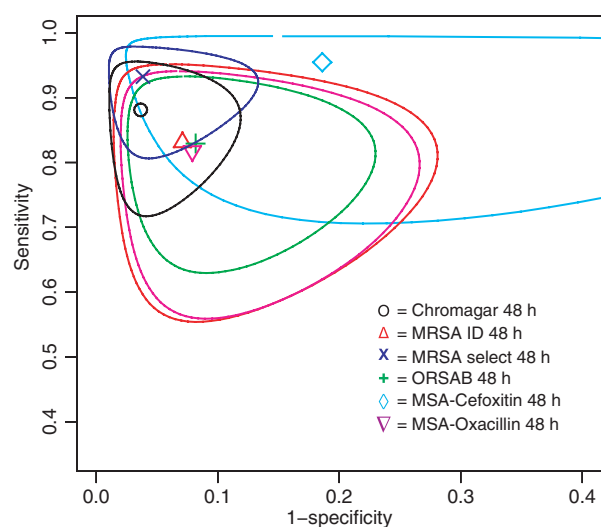


FIG. 7. Bivariate summary estimates of sensitivity and specificity for all six 48-h culture (both chromogenic and nonchromogenic) tests evaluated and the 95% confidence ellipses around these mean values. To improve readability, the confidence ellipse of MSA-Cefoxitin 48 h (in light-blue) is not fully covered.

analysis using mathematical modelling can inform decision-makers on the interaction and trade-offs between price, sensitivity, specificity and TAT within different screening strategies.

In conclusion, this meta-analysis showed statistically significant differences in diagnostic accuracy between several tests evaluated. A reduction of the incubation time on chromogenic media, from 48 to 18-24 h, increases specificity, but reduces sensitivity. Inclusion of non-nasal samples slightly

(although nonsignificantly) reduced sensitivity, but did not change specificity.

Author Contributions

JML and GAAH are the principal investigators of this study. PP supervised the statistical analysis. MJB critically reviewed several versions of the manuscript and provided information on the clinical aspects of MRSA detection methods. MJP supervised this study.

Transparency Declaration

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